a third of these have thickened skin on the dorsum of the fingers and hands. Most recently, it has been observed that limited joint mobility of the hands is also a common finding in adults who have diabetes mellitus.

Does this new finding have any significance in regard to other parameters of diabetes? Most reports suggest a correlation of these hand findings with diabetic retinopathy. It has also been suggested that this dermal thickening is the result of glycosylation of collagen, which results in a relative resistance of collagen to collagenase and a stiffer, stronger collagen. Increased glycosylation of collagen and the resulting changes in the biomechanical properties of this molecule occur normally with aging, and the occurrence in patients with diabetes is consistent with accelerated aging. Reports on the correlation of the diabetic hand with control of diabetes have, however, been conflicting.

In summary, skin and joint changes of the hands are fairly common findings in patients with diabetes mellitus. Along with other prognostic indicators, these changes should be sought on physical examination of diabetic patients. Although it is tantalizing to consider that hyperglycemia resulting in collagen glycosylation may be responsible for both dermal thickening and internal complications of diabetes mellitus, such a connection is far from proved. For clinicians today, the diabetic hand syndrome remains a relatively common and interesting finding that has a probable correlation with retinopathy.

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Malignant Melanoma—Recognition of New Histologic Variants With Favorable Prognosis

SINCE THE ORIGINAL WORK on ocular melanoma showed that patients with nonpigmented spindle cell melanomas have a better prognosis than those with other types, several studies have been done to determine which clinical and histologic variables have prognostic significance for primary cutaneous melanoma.

Results of these studies have uniformly indicated thickness to be a major prognostic indicator, but data regarding the significance of other histologic features remain less than clear, in part because of differences between studies and in part because some studies were based on the premise that lentigo maligna melanoma has a better prognosis than superficial spreading melanoma, which has a better prognosis than nodular melanoma. Therefore, cell types most often seen in patients with lentigo maligna melanoma were inferred to indicate a better prognosis.

In a recent study by Koh and co-workers, of 48 cases of lentigo maligna melanoma matched with non-lentigo maligna melanoma for site and thickness, a Cox multivariate analysis selected only thickness in predicting death. As with other large multicenter cooperative studies, this study indicated little or no independent impact of histologic features on the prognosis of patients with clinical stage I melanoma (primary melanoma with no clinical evidence of metastasis).

Histologically, lentigo maligna melanoma and superficial spreading melanoma are characterized by a radial growth phase or the horizontal spreading of malignant cells within and just beneath the epidermis (Breslow's level less than 0.76 mm or Clark's level I and II, indicating a good prognosis). In time, a vertical growth phase supervenes, expanding to more than 1.25 mm or Clark's level III, IV or V, indicating an increasingly worse prognosis. In nodular melanoma a vertically expanding nodule is characteristic and the radial growth phase may not be recognizable.

There is a histologic variant of malignant melanoma called minimal deviation melanoma that may prove to be the exception to the rule. This uncommon nevomelanocytic tumor appears clinically as a Spitz nevus, hemangioma or malignant melanoma. They occur on any body site, at any age and may arise in preexisting dermal nevi or in the midst of a congenital nevus. Histologically, cells making up an expansile nodule of the vertical growth component show mitotic figures but very minimal cytologic atypism such that, if the nodule arises in a nevus, differentiation of malignant from benign cells may be very difficult. When the nodule is located within Clark's level II, the lesion is called a borderline minimal deviation melanoma, borderline indicating the biologically benign nature of the lesion unless it penetrates to level III where its biologic behavior is unpredictable. (Other melanomas would predictably have a progressively worse prognosis).

Muhlbauer and colleagues recently reported a study of 21 patients with minimal deviation melanoma. The mean tumor thickness was 3.6 mm, or level V. After 57 months, only two of three deaths could be attributed to melanoma, the other patients being disease free.

Because of the less aggressive nature of these lesions, the authors express hesitation at assigning a Breslow or Clark's level because of therapeutic implications (local excision versus wide excision with possible lymph node dissection).

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A Micrographically Controlled Operation for Difficult Skin Cancers

ABOUT 40 YEARS AGO, Mohs developed a technique to remove skin cancers that has been modified to obtain a fresh tissue specimen for microscopic examination with careful mapping, now called micrographically controlled surgery.

Skin cancer accounts for 25% of all cancers in humans,

the most common of which are basal cell carcinomas that occur on sun-exposed areas of the head and neck. Persons with fair skin living in lower latitudes are at increased risk for the development of skin cancer. The incidence of skin cancer doubles for each 3°45′ of latitude toward the equator. Treatment includes curettage and electrodesiccation, excision, irradiation, cryosurgery and micrographically controlled surgical excision of tumors with high recurrence rates.

Technique

The micrographically controlled operation is done under local or regional anesthesia. The tumor is debulked. The specially angled saucerized tissue specimen is cut horizontally across the bottom in serial frozen sections. The entire undersurface and the epidermal margin of the excised tissue can be seen microscopically and mapped. One is then able to remove only tissue in which the tumor is microscopically persistent, allowing maximal preservation of normal skin. Mohs's surgical procedure is used for certain primary basal cell carcinomas and squamous cell carcinomas, most recurrent skin cancer, verrucous carcinoma and other paracutaneous neoplasms in the mouth and sinuses.

The criteria for selecting Mohs's procedure over other modalities in treating cases of primary basal cell carcinoma include tumor location, histologic analysis, size (greater than 2 cm) and clinical characteristics. In cases of recurrent basal cell carcinoma, a micrographically controlled surgical procedure is clearly the treatment of choice. The criteria are comparable for the less frequently occurring squamous cell carcinomas.

Tumor location is important. Areas of high recurrence are embryonic planes including the nasal septum, the nasal ala, the junction of the nasal ala with the nasolabial fold, the periorbital region and the periauricular region extending to the temple. Basal cell carcinoma follows the paths of least resistance, along facial planes, periosteum, perichondrium and eyelid tarsal plate, spreading along these structures before invading.

Primary basal cell carcinomas have several histopathologic characteristics with differing biologic behavior. Morpheaform or sclerotic basal cell carcinomas, multicentric infiltrating tumor or the keratinizing aggressive basal cell carcinoma (metatypical carcinoma) can be clinically aggressive with higher recurrence rates than nodular basal cell carcinomas. Sclerotic basal cell carcinoma can have a large subclinical extension, especially on the temple and forehead.

A third factor is tumor size. For tumors larger than 2 cm, Mohs's operation is generally recommended. The cure rate for Mohs's procedure is 98.6% for tumors between 2 cm and 3 cm in diameter and 90% for tumors greater than 3 cm in diameter. Most basal cell carcinomas are well-defined nodules. However, some have ill-defined clinical borders exhibiting a multicentric nature. In this situation Mohs's operation might be considered a treatment of choice if a large, clinically judged excision is not appropriate.

Incompletely excised basal cell carcinomas have variable recurrence rates: 82% on eyes, ears and nose and 25% on the remainder of the head and neck. Mohs's surgical procedure has a success rate of about 96% for recurrent basal cell carcinomas compared with the 50% success rate of other modalities. It has the additional advantage of preserving the maximal amount of normal skin.

In conclusion, location, histologic characteristics, size and clinical nature of a primary skin cancer are important in deciding the most effective treatment modality.

New techniques to improve the cure rate are immunofluorescent and immunoperoxidase staining antibodies to keratin. This keratin antibody staining in frozen section appears to be an effective method of distinguishing strands of cancer cells in poorly differentiated squamous cell carcinoma or morpheaform basal cell carcinoma from inflammatory cells.

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Minoxidil

MINOXIDIL IS a potent peripheral vasodilator used in treating patients with hypertension. When taken orally, the drug causes a reversible, nonvirilizing hypertrichosis in most patients. In women, the increased hair growth involves the face, shoulders and limbs and, in men, there is a generalized increase of body hair.

Topical minoxidil, not yet approved by the Food and Drug Administration, is being studied in large, multicenter projects to assess the drug's efficacy and safety when applied to the scalp of patients with alopecia areata and those with androgenetic alopecia.

In men, women and children with alopecia areata affecting 25% to 99% of the scalp, topical application of minoxidil produces hair growth in about 30% of the patients after a year of treatment. The results with 1% and 3% topical minoxidil are similar. After two and three years of topical treatment, it is possible that a higher percentage of patients, including some with 100% scalp hair loss, will grow cosmetically acceptable hair. One study has shown a substantially greater response rate using 5% minoxidil in cases of alopecia areata.

In men with androgenetic alopecia, cosmetically acceptable hair growth is achieved in about 30% after twice-a-day application of minoxidil for one year. Both 2% and 3% topical minoxidil produces similar results in patients with androgenetic alopecia. Hair growth begins after four to six months of treatment. The presence of pigmented hairs longer than 1 cm is a favorable indicator for response; the greater the density of such miniaturized hairs, the more likely the patient will respond well to topical application of minoxidil. In addition, the shorter the duration of the balding process and the smaller the balding area, the better the likelihood of a cosmetically acceptable response.

Topical minoxidil appears to be safe in those with a normal cardiovascular state. Side effects have consisted mainly of mild skin irritation in only a few patients.